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Effect and Side Effect of Stimulant/Methylphenidate on Children and Adolescents with ADHD: The Qatar Experience

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Abstract

Objectives: Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurobiological disorder of childhood. The Diagnostic Statistical Manual of Mental Disorders describes ADHD as impairing symptoms of inattention, impulsivity and hyperactivity (DSM-V, 2013). ADHD has been associated with a broad range of negative outcomes for children including academic underachievement and social difficulties. The objective of this study was to look at the positive effects and side effects of methylphenidate in academics and behaviors among school aged students.

Methods: 101 patients who fulfilled the diagnostic criteria for Attention Deficit Hyperactivity Disorder according to the DSM-V were randomly selected to participate in this study. The patients were assessed by a Pediatrician. The SNAP-IV questionnaire was completed by parents and teachers. A questionnaire was devised by the researchers to gather additional information with regards to improvement in overall quality of life following medication and improvement in academic performance and behavior according to parents and teachers. Around half of them were followed for less than a year and the remaining for more than that.

Results: Our results showed 91% had marked improvement in overall academic performance after starting medication. 88 % reported improvement in behavior. 72% reported at least one side effect with the most common being decreased appetite (43%) and trouble falling asleep (26%).

Conclusion: Our data revealed more than half of the patients experienced at least one side effect; however, most patients reported that intervention with medication had a positive impact, with marked improvement in academics and behavior.

Keywords: ADHD; Adolescent; Children; Effects; MPH

Abbreviations

ADHD : Attention Deficit Hyperactivity Disorder

MPH : Methylphenidate

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is the most common childhood-onset neurobiological disorder that affects school learning and socialization. The Diagnostic Statistical Manual of Mental Disorders (DSM-V) describes ADHD as typified by pervasive and impairing symptoms of inattention, impulsivity and hyperactivity [1]. It is estimated to affect between 9.5 and 16% of all school age children [2-4]. ADHD has a negative impact on multiple domains of Quality of Life (QOL) for children, adolescents and their families including social, academic and family life. Thus, early detection and management is essential to improve overall outcome.

Attention-Deficit Hyperactivity Disorder (ADHD) is characterized by age-inappropriate impulsivity, impaired attention, hyperactivity or a combination [5]. These behaviors have a broad range of negative outcomes for patients and their families. The symptoms of ADHD have been shown to negatively impact children's self-esteem and social function which includes their behavior, academic success and quality of life and their families

[5,6]. Negative outcomes of untreated ADHD.

ADHD has been associated with a broad range of negative outcomes for children such as academic underachievement including lower grades, attendance, graduation rate and even dismissal from school. Families of children with ADHD experience increased stress. A person with ADHD could be affected as an adult when it comes to success at work and relationship forming [7-9]. Furthermore, a study of the Cost of Illness (COI) estimated annual COI of ADHD in children and adolescents at between $12,005 and $17,458 per individual which included health care costs, education (special education), and juvenile justice [10]. A European study found similar cost of illness results [11].

Academic Failed/Lower Grades

Loe and Feldman's (2007) [12] review of the literature found in longitudinal studies that academic underachievement associated with ADHD was persistent and began early in life. Children with ADHD repeated the academic year, achieved lower ratings in all subjects on report cards and performed comparatively poor in standardized tests than the control group. A further review of the literature by Daley and Birchwood (2010) [13] looked at the relationship between ADHD and academic performance at different developmental stages; they found that students taking stimulant medication did better academically than those with ADHD not receiving medication. Meta-analysis has demonstrated that the use of Methylphenidate (MPH) medication with children with ADHD improved math and reading abilities of these students but had a much greater improvement on their behavior [5]. Methylphenidate has been shown to improve academic performance in Primary school children and interestingly found more improvement the later the child started medication. Furthermore, it was found that these children were still below that of typical peer performance [14].

Attendance/Graduation

School histories illustrated persistent problems in socialization with students with ADHD taking more years to complete high school and having lower rates of college attendance and graduation. [12]. A European meta-analysis showed that children with symptoms of ADHD had increased dropout rates compared to their counterparts not experiencing these symptoms and therefore this added to lower graduation rates [15].

Lack of Success as Adult

Untreated ADHD is a principal cause of lack of success for many adults. Research has established that teenagers and young adults with untreated ADHD have less probability of attending college or university, they get in trouble with the law more frequently, are more frequently found in prisons, experience more divorce or difficulty with relationship forming and durability and do not achieve their potential at workplace. The social and emotional impairments associated with ADHD affect the quality of life for these adults and their families. If left untreated, these people could become a burden on their family and society [11,12,16-21].

Family Wellbeing

Family wellbeing i.e. relationships within families and between siblings was often reported lower for those with untreated ADHD compared to those who do not have ADHD [22]. In a large cross-sectional study of QOL for children with ADHD, parents' response demonstrated that QOL of children with ADHD was positively linked with treatment [6]. In a review of the literature, researchers concluded that ADHD seriously compromises quality of life, especially when seen from parents' perspective. Reports of the family's QOL and well-being were more compromised where increased symptoms of ADHD were experienced by the child. They also found evidence that QOL of the child improved with the use of stimulant medication [23].

Home Disruption -Siblings

Kendall (1999) [24] in her qualitative study of parent and sibling accounts in families with at least one child diagnosed with ADHD asked siblings to write in diaries once a week for eight weeks and in-depth interviews were conducted with the siblings and parents. Results of these interviews found that disruption to home life was the most common and significant problem. Children described their family life as chaotic, full of conflict and exhausting. Some children stated that living with a sibling with ADHD meant never knowing what to expect next and hopelessness that it would never change. More recent studies of sibling perceptions also found the siblings without ADHD believed themselves to be negatively impacted by having a brother or sister at home with ADHD that received different treatment, discipline and more attention. This need for extra time and assistance often lead to feelings of being ignored. Findings signified that a child with ADHD does have a huge impact on the family. Parent Stress

Anastopoulos, et al.'s (1992) [16] study of parent stress and ADHD found that parents of children with ADHD scored extremely high, above the 90th percentile, on a well-known parenting stress index. Parental stress or quality of life was also reported to be poorer for those with untreated ADHD compared to those who do not have ADHD. Mothers found inattention and opposition most stressful but not hyperactivity, whereas, fathers were more distressed by opposition and aggression [20]. Muñoz-Silva, et al (2017) [25] also found that the association between ADHD and parent stress was attributable to children's conduct problems and the negative impact on the family's social life. Overall, parent and family stress impacts quality of life when there is a child with ADHD in the family [22].

Financial Burden

Burd, et al (2003) [26] found that annual mean direct treatment costs for children aged between 0-21 years old with ADHD was $870 compared to $663 for controls. Leibson, et al (2001) [27] longitudinal study found that median direct treatment costs of children aged between 5-19 years old with ADHD was $6,158 compared to $2,780 for controls. This study was conducted over 9 years. Mandell, et al (2003) [28] looked at children aged between 3-15 years old with ADHD and no psychiatric disorder over 3 years. The mean direct treatment cost was $4,891 for ADHD patients compared to $221 for patients with no psychiatric disorder.

We know that up to 70% of those diagnosed with ADHD in childhood continue to have symptoms in adulthood [29]. Secnik et al (2005) [30] and Swensen et al (2003, 2004) [31,32] compared costs of care for adults with ADHD with controls matched on age, sex, area or residence, insurance cover and found that those with ADHD have considerably higher annual medical costs than matched controls ($4,929 to 5,651 vs $1473 to $2,771). Identification No laboratory tests reliably predict ADHD [33]. Procedure for identifying a person with ADHD starts at home or at school. Usually parents or teachers identify that there is a behavioral or academic problem with the child. Sometimes a school psychologist assists in this diagnosis, but Qatari schools generally do not have the luxury of these services. Frequently, school administrators or specialized teachers become involved to assist a child with ADHD difficulties. Sometimes parents take their child to a pediatrician, psychiatrist, or private psychologist for assistance.

Treatment

Treatment of ADHD usually involves a multi-modal approach which includes pharmacological and non-pharmacological options. Stimulants are the first drug of choice in the management of ADHD symptoms [14]. Methylphenidate (MPH) is the first line treatment and has been used for over 50 years [34]. It is the most commonly prescribed drug treatment for this disorder [35]. MPH medications are an effective way of managing symptoms of ADHD such as improving attention span, reducing distractibility, improving memory, reducing impulsivity and hyperactivity [36,37].

There is broad public concern about rates of stimulant prescription for ADHD treatment and stimulant usage remains a contentious issue. With the plethora of negative information and articles in the popular press and on the internet with respect to the number of children being prescribed medication for behavioral issues, parents are often hesitant to agree to medication for their child who is seen to have a behavioral problem that some believes to be caused by the school [38]. In her study, Arcia (2004) [39] found that mothers preferred treatment other than medication for their child with ADHD. In a study with parents of children taking stimulant medications for ADHD, 55% were reluctant to give their child medication based on information in the local press and 38% thought that too many children receive medication for ADHD [40]. Other researchers have found similar results when examining parents' resistance to give their children medication for behavioral difficulties [41-43].

The medically accepted treatment of stimulant medication is highly effective but does not always provide complete amelioration of the symptoms of ADHD, especially the focus and attention required in many school settings [44]. In addition, there are those children for whom stimulant medication is not providing the desired result or who experience side effects from the medication and do not or cannot take medication. Thus, the child is left without the required support that they may need to become a successful productive student and member of society. Furthermore, without support, the child ends up less successful in school and is often alienated socially with law enforcement troubles in adolescence [41,45-47].

Side Effects of Methylphenidate Use in Children

There is a wide range of side effects experienced by children and adolescents when taking stimulant medication ranging from lack of appetite to increased aggression and somatic symptoms such as headache and gastrointestinal complaints. Participants in Efron et al.'s (1997) [48] study reported side effects like prone to crying (71%), staring (62%), anxiety (61%), sadness (56%), nail biting (45%), euphoria (43%) and less talking (42%). In another study, Haertling et al. (2015) [49] reported only 13.7% of participants experienced side effects. Yet Khajehpiri et al. reported 100% of their participants experienced side effects. Thus, it is important to look at the side effects experienced in our study and to ensure that we are aware and can assist children and families who experience these as it may deter continuation of medication treatment for children. Why this research is needed: Qatar experience. The prevalence of ADHD in school age children in Qatar has been shown to be like worldwide prevalence [50]. However, there are no studies examining ADHD treatment outcomes in Qatar. There are a limited number of studies from neighboring countries in the region on ADHD. Most of these studies explore epidemiology [51-53]. A study that included Egypt, Lebanon, and the U.A.E. explored predictors for treatment outcomes of MPH but did not examine the academic outcomes [54].

An estimate of prevalence in Qatar suggests up to 19% of Qatari children aged 6-12 years in government schools have moderate to high levels of ADHD according to teacher rating scales [50,55]. This equates to more than 15000 Qatari students who may or may not be receiving treatment for a potentially debilitating disorder that can limit a person's success in life. A study by Rhee and Waldman (2002) [56] established familial or biological links in people with ADHD. In their clinic-referred sample, 34-40%

of the subjects with ADHD reported a family history of ADHD compared to 8% of control subjects. Considering these studies of familial links there is support for further research in Qatar where consanguineous marriage is common.

Materials and Methods

Study Statement

The primary focus of this study was to examine whether MPH improves the behavior, academic success and family wellbeing of those affected with ADHD in Qatar. We also explored the adverse effects profile as a secondary focus. We aimed to explore the effects of MPH use in a comprehensive setting including the home and the academic environment as reported by teachers and parents. We hypothesized that the use of MPH will improve attention, reduce hyperactivity and improve academic achievement and family wellbeing. We also hypothesized that the side effect profile for MPH will be like those in other countries - decreased sleep and appetite being the most common.

Participants

Participants in this study included 101 patients who fulfilled the diagnostic criteria for ADHD according to the DSM-V and had inattention, behavioral problems, hyperactivity, impulsivity and/or aggressive behavior along with inattention affected academic difficulties due to ADHD. Participants were enrolled at Hamad Medical Corporation outpatient clinic. Seventy-five percent of participants were males and 25% females. Participants' age ranged from 5 - 18 years old and they were all enrolled in Qatar's Government schools. The demographics of the patient population are outlined in (Table 1). Along with ADHD, participants were also diagnosed with co-morbidities, the main ones being learning disability 17 (16.6%), autism spectrum disorder 4 (3.9%), anxiety 4 (3.9%) and depression 2 (2%). The presenting symptoms of the patient population are mentioned in (Figure 1). DSM-V The DSM-V ADHD checklist includes a list of nine symptoms of inattention and nine symptoms of hyperactivity/impulsivity [57]. It is the standard measure for ADHD diagnosis. Based on the DSM-V criteria, a child must display six out of the nine symptoms in at least one of the two areas or both areas (inattention, hyperactivity-impulsivity, inattention and hyperactivity-impulsivity) to be diagnosed with ADHD. SNAP IV Swanson, Nolan and Pelham SNAP-IV Questionnaire is an 18-item questionnaire measuring the full DSM-V criteria of ADHD (9 items questioning inattention and 9 items questioning hyperactivity) that has high reliability and validity [58]. It uses a four-point scale of frequency for each item (3 = very much, 0 = not at all). A pilot of all the survey questions was conducted prior to the study to ensure the questions are readable and comprehensible, and that the Arabic version was clearly understood. Researcher designed questionnaire.

Patient Demographics	N	Frequency (Percentage)	
Gender			
Male	101	76	-75.20%
Female		25	-24.80%
Nationality			
Qatari	101	37	-36.6
Non-Qatari		64	-63.4
Age at enrollment			
5 years		1	-1%
6-10 years	101	46	-45.50%
11-15 years		45	-44.60%
>16 years		9	-8.90%
Age at diagnosis			
5 years	97	61	-59.80%
6-10 years		31	-32%
11-15 years		5	-5.20%
Family history of behavioral problems			
Yes	101	58	-57.40%
No		39	-38.60%
Not known		4	-4%
Father's level of education			
Not completed high school		13	-12.90%
High School graduate	101	28	-27.70%
Graduate degree		39	-38.60%
Post graduate degree		18	-17.80%
Unknown		3	-3%
Mother's level of education			
Not completed high school		21	-20.80%
High School graduate	101	24	-23.80%
Graduate degree		39	-38.60%
Post graduate degree		15	-14.90%
Unknown		2	-2%
Consanguinity			

Yes	100	39	-39%
No		57	-57%
Not known		4	-4%
Patient's IQ			
Not done		64	-62.70%
High average (110-119)			0 (0)
Average (90 - 109)	99	8	-7.80%
Lower average (80 - 89)		13	-12.70%
Borderline (70 - 79)		14	-13.70%
Extremely low (69 and below)		3	-2.90%

Table 1: Patient Demographics.

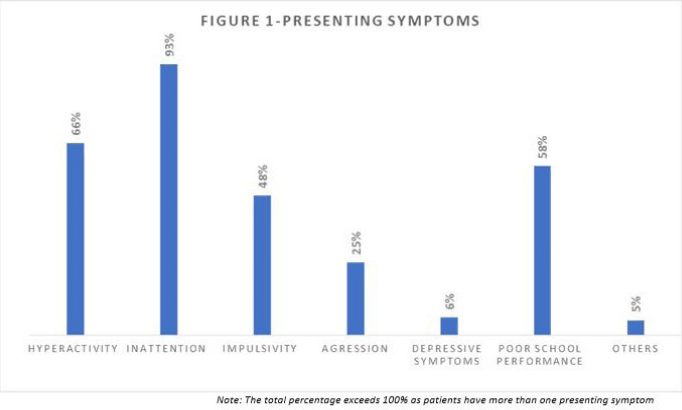

Figure 1: Presenting Symptoms.

A questionnaire was devised by the researchers to gather additional information with regards to improvement in overall family wellbeing and academic performance. Questions regarding academic performance included scores related to reading, mathematics and written expression taken from the NICHQ Vanderbilt assessment scale [59].

Procedure

The parents signed a statement of informed consent and gave medical history as well as completed the SNAP-IV questionnaire during their initial appointment. The student's teachers completed a pretreatment SNAP-IV questionnaire shortly after the initial clinical appointment. Those children and adolescents who were diagnosed with ADHD were then started on short acting methylphenidate 0.3 mg/kg to the nearest 2.5 mg using 5 and 10 mg tablets or extended-release MPH with doses ranging 18 - 54 mg. Dosages were titrated according to feedback from parents and school reports. Patients were then followed according to the Stimulant Drug Protocol [60]. Around half of them were followed for less than a year and the remaining for more than that. Once done, patients' parents were asked to fill out the SNAP-IV survey form and researcher designed questionnaire. Statistical analysis

Mean improvement in the score for quantitative variables (inattention score, hyperactivity-impulsivity score, and ADHD Combined score) between the pre-medication SNAP-IV and post medication SNAP-IV were analyzed using paired t-tests and the results were presented with respective p-value and associated 95% confidence interval. Associations between two or more categorical variables were examined using Chi-square test or Fisher exact test as appropriate. All p- values presented were two-tailed, and p values <0.05 was considered as statistically significant.

Results

Treatment

Following the confirmation of an ADHD diagnosis, 53.5% of the patients were started on long-acting methylphenidate (Concerta) while 17.2% were prescribed short-acting methylphenidate (Ritalin). Another 16.2% of the patients were started on a combination of long-acting methylphenidate for the day, followed by a dose of short-acting methylphenidate to cover the afternoon time. The remaining 13.1% of the patients were on a combination therapy of methylphenidate and a second non-stimulant medication, which included atomoxetine or antidepressants. (Figures 2-4) provide more information on type, duration and frequency of treatment. Effect of treatment

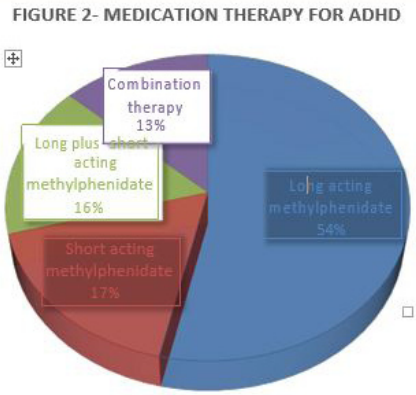

Figure 2: Medication Therapy for ADHD.

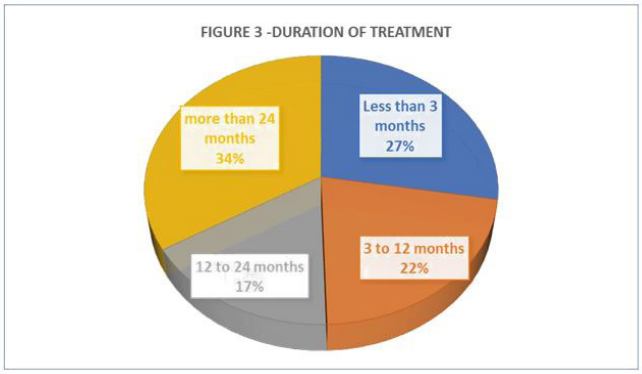

Figure 3: Duration of Treatment.

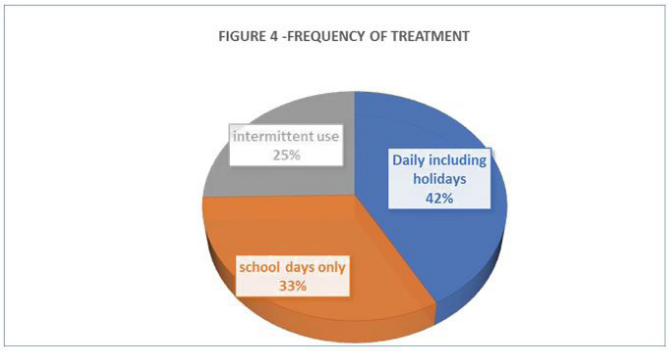

Figure 4: Frequency of Treatment.

The six months follow up appointment revealed that 91% of the children had remarkable improvement in their overall academic performance after starting medication as reported by the researcher's questionnaire. Parents reported based on teachers' feedback that 88% improved in writing skills, 87% improved in reading skills, and 82% improved in arithmetic as shown in (Figure 5). Furthermore, 84 % reported improvement in their overall family wellbeing, while 85 % reported improvement in behavior as demonstrated in (Figure 6).

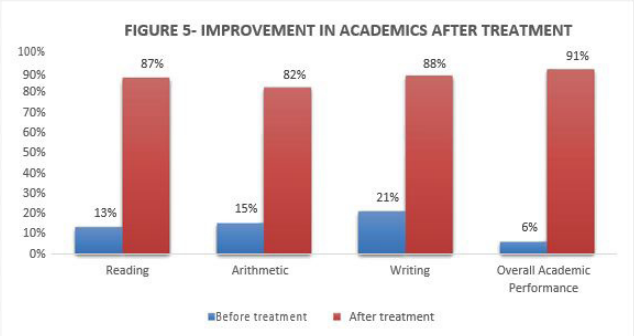

Figure 5: Improvement in Academics after treatment.

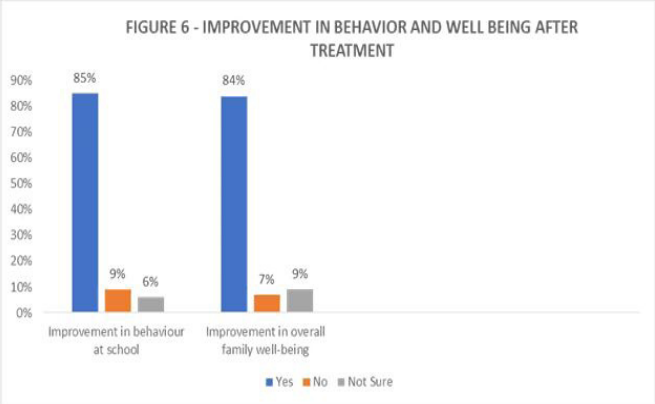

Figure 6: Improvement in Behavior and well-being after treatment.

SNAP-IV questionnaire-pre and post treatment (Parent questionnaire) in (Table 2) Paired t-test was used to compare mean score between pre and post intervention. The mean inattention score was significantly reduced at post intervention (0.95, +/- 0.46, $p < 0.001$) compared to pre-intervention (1.96, +/- 0.64, $p<0.001$). The mean hyperactivity score was significantly reduced at post intervention (0.84, +/- 0.59, $p<0.001$) compared to pre-intervention (1.54, +/- 0.92, $p<0.001$). The mean combined score was significantly reduced at post intervention (0.89, +/- 0.48, $p<0.001$) compared to pre-intervention (1.75, +/- 0.65, $p<0.001$). Side effects of treatment

	Pre	Post	P-Value
Inattention	1.96 +/- 0.64	0.95 +/- 0.46	<0.001
Hyperactivity	1.54 +/- 0.92	0.84 +/- 0.59	<0.001
Combined	1.75 +/- 0.65	0.89 +/- 0.48	<0.001

Table 2: Mean scores for each type of ADHD, pre and post treatment.

Seventy-Five percent of the participants reported side effects after starting treatment. Twenty-seven reported only one side effect, while 45% reported 2 or more side effects and remaining 25% experienced no adverse effects after starting medication. The most common reported side effect was poor appetite in 42% followed by poor sleep in 25% and increased aggression after the medication wore off in 22%. Nineteen percent complained of gastrointestinal symptoms and another 19% suffered from headaches (Figure 7) provides more details about side effects as reported.

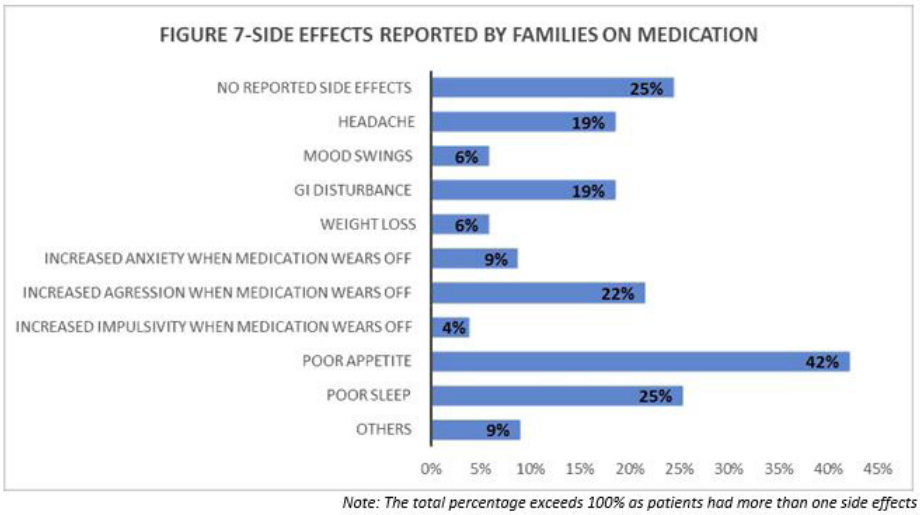

Figure 7: Side Effects reported by families on medication.

Upon comparison of patient characteristics with regards to the likelihood of experiencing side effects, girls were found to be more vulnerable with 80% experiencing one or more side effect compared to 63% of boys however the difference was not statistically significant (p=0.288) due to the small sample size. Patients who were started on both long and short-acting methylphenidate simultaneously were more likely to experience one or more side effects (94%) when compared to their peers who were taking only a single stimulant or any other form of combination therapy, (p=0.345). Seventy-eight percent of the children who were on treatment for less than 3 months experienced side effects. This dropped to around 63% in patients who had been on medication between 3-24 months and increased again to 76.5% among those on medication for more than 2 years. Overall, no statistically significant differences were noted in the side effects between patients in terms of age, gender, diagnosis, or the type, duration and frequency of medication. Results may have been more statistically significant with a larger population. (Table 3) describes this information in detail.

Patient Characteristics	Experienced one or more side effects	P value
Gender		
Male	46/73 (63%)	0.288
Female	20/25 (80%)	
Age		
3-5 years	0/1 (0%)	
6-10 years	32/45 (71.1%)	0.392
11-16 years	34/45 (75.6%)	
Above 16 yrs.	6/9 (66.7%)	
Diagnosis		
ADHD	53/72 (73.6%)	0.538
ADHD with comorbidity	19/28 (67.9%)	
Medication		
Long acting MPH	35/53 (66%)	
Short acting MPH	12/17 (70.6%)	0.345
Long and Short acting MPH both	15/16 (93.7%)	
MPH with other non-stimulant medications*	9/13 (69.2%)	
Frequency of use		
Daily (incl long holidays)	9/12 (75%)	0.3
School Days	41/53 (77.4%)	
Intermittent Use	22/35 (62.9%)	
Treatment Duration		
Less than 3 months	22/28 (78.6%)	
3 to12 months	14/22 (63.6%)	0.54
12 to 24 months	10/17 (62.5%)	
More than 24 months	26/34 (76.5%)	
Compliance		
Good	65/90 (72.2%)	0.865
Poor	7/10 (70%)	

Table 3: Patient Characteristics and Side effects.

Discussion

The results of this study on the effects of MPH for children and adolescents with ADHD in Qatar government schools demonstrate that children and adolescents who took MPH improved overall in academics, behavior and family wellbeing. Improvement occurred regardless of the prescription whether MPH or combination therapy. These results are consistent with similar international studies [5].

There was marked improvement in symptoms of inattention and hyperactivity when comparing scores for untreated ADHD and after starting treatment at a six month follow up appointment. There was also marked improvement in academics (reading, writing and math) once treatment began. The same was also observed by Daley and Birchwood (2010) [13]. Academic improvement is one of the key targets for measuring the success of treatment for those with ADHD. Previous literature found that those prescribed MPH improved their math and reading abilities [5]. We also know that untreated ADHD results in lower ratings in school subjects on report cards and poorer grades on standardized tests [12]. Although in this study a comparison of standardized grades was not assessed, feedback from teachers and parents reported academic improvements.

Family stress and quality of life due to dealing with a child with ADHD are often reported in the clinic setting. Here we demonstrated significant improvement in family stress and quality of life with improved social functioning outcomes between pre and post-treatment assessments as reported by parents. Thus, it is important for the medical profession to understand that social functioning and family life improves with stimulant intervention for children with ADHD.

Seventy-two percent of participants reported that they experienced side effects after taking MPH whether taking long or short acting medication. It is important to note that females reported more side effects compared to males and patients who were started on a combination of both long and short acting MPH simultaneously experienced more side effects than those who were only started on one MPH. The high rates of side effects experienced in this study are like what was reported by Khajehpiri et al. Seventy-six percent of patients complained of side effects after 6 months of use which indicates the need for a longitudinal study examining the duration of side effects experienced.

Limitations of this study include not using standardized assessments to compare academic improvements pre and post treatment. Additionally, although the SNAP-IV questionnaire is validated, it was not validated on a Middle Eastern population and therefore results may not be generalized.

This study enhanced and expanded on the results other studies found in Qatar regarding children with ADHD [50,55]. It brings forward a condition that is little talked about and often not recognized in this culture and provides Arabic parents with evidence-based resources to access in their own culture when they have questions about treatment for their child with ADHD. It will assist Qatari health professionals in their treatment plan for children with ADHD and may provide some evidence that they need to consider suggesting or offering medical or other treatments for children with ADHD.

Future research needs to be conducted to examine exactly what aspect of educational performance is improved and quantify those with standardized assessments to have more objective goals for family and schools. Ultimately, prescribing MPH seems to improve academic performance by improving attention and behavior in terms of hyperactivity and impulsivity as well as family wellbeing, which all have positive outcomes for the children, parents and the schooling system.

Conclusion

This study showed marked improvement in overall academic performance, quality of life and behavior after starting medication. More than half reported at least one side effect with the most common being decreased appetite and insomnia.

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